IN THE CLAIMS

Please cancel claims 1-85. Please add the following new claims 86-107.

86. (New) A humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from acceptor immunoglobulin heavy and light chains, which humanized immunoglobulin specifically binds to an antigen, wherein said humanized immunoglobulin comprises at least three amino acids from the donor immunoglobulin heavy chain framework outside the Kabat CDRs that replace the corresponding amino acids in the acceptor immunoglobulin heavy chain framework at positions in the immunoglobulins where:

(I) the amino acid is immediately adjacent to one of the CDRs, or

(II) the amino acid is capable of interacting with the CDRs, or

(III) the donor amino acid is typical at its position for human immunoglobulin sequences, and the replaced amino acid is rare at its position for human immunoglobulin sequences,

wherein at least one of said amino acids is capable of interacting with CDRs 2 or 3.

87. (New) A humanized immunoglobulin according to claim 86 , wherein said humanized immunoglobulin binds to the antigen with an affinity constant of at least 10^8 M^{-1}.

88. (New) A humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from acceptor immunoglobulin heavy and light chains, which humanized immunoglobulin specifically binds to an antigen with an affinity constant of at least about 10^8 M^{-1} and no greater than about four-fold that of the donor immunoglobulin, wherein said humanized immunoglobulin comprises at least three amino acids from the donor immunoglobulin heavy chain framework outside the Kabat CDRs that replace the corresponding amino acids in the acceptor immunoglobulin heavy chain framework, and each of these said donor amino acids:

(I) is immediately adjacent to one of the CDRs, or

(II) is capable of interacting with the CDRs,

wherein at least one of said amino acids is capable of interacting with CDRs 2 or 3.

89. (New) A humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from acceptor immunoglobulin heavy and light chains, which humanized immunoglobulin specifically binds to an antigen with an affinity constant within about four-fold that of the donor immunoglobulin, wherein said humanized immunoglobulin comprises at least three amino acids from the donor immunoglobulin heavy chain framework outside the Kabat CDRs that replace the corresponding amino acids in the acceptor immunoglobulin heavy chain framework, and each of these said donor amino acids is capable of interacting with the CDRs, wherein at least one of said amino acids is capable of interacting with CDRs 2 or 3.

90. (New) A humanized immunoglobulin according to any one of claims 86 through 89, wherein said humanized immunoglobulin is an antibody tetramer, Fab, or $(Fab')_2$.

91. (New) A humanized immunoglobulin according to any one of claims 86 through 89, which is substantially pure.

92. (New) A pharmaceutical composition comprising a humanized immunoglobulin according to claim 91 and a pharmaceutically acceptable carrier.

93. (New) A humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from acceptor immunoglobulin heavy and light chains, which humanized immunoglobulin specifically binds to an antigen, wherein said humanized immunoglobulin comprises at least one amino acid from the donor immunoglobulin light chain framework outside the Kabat CDRs that replaces the corresponding amino acid in the acceptor immunoglobulin light chain framework, and said donor amino acid:

(I) is immediately adjacent to one of the CDRs, or

(II) is capable of interacting with the CDRs, or

(III) is typical at its position for human immunoglobulin sequences, and the replaced amino acid is rare at its position for human immunoglobulin sequences.

94. (New) A humanized immunoglobulin according to claim 93 , wherein said humanized immunoglobulin binds to the antigen with an affinity constant of at least 10^8 M^{-1}.

95. (New) A humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from acceptor immunoglobulin heavy and light chains, which humanized immunoglobulin specifically binds to an antigen with an affinity constant of at least about 10^8 M^{-1} and no greater than about four-fold that of the donor immunoglobulin, wherein said humanized immunoglobulin comprises amino acids from the donor immunoglobulin light chain framework outside the Kabat CDRs that replace the corresponding amino acids in the acceptor immunoglobulin light chain framework, and each of these said donor amino acids:

(I) is immediately adjacent to one of the CDRs, or

(II) is capable of interacting with the CDRs.

96. (New) A humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from acceptor immunoglobulin heavy and light chains, which humanized immunoglobulin specifically binds to an antigen with an affinity constant within about four-fold that of the donor immunoglobulin, wherein said humanized immunoglobulin comprises amino acids from the donor immunoglobulin light chain framework outside the Kabat CDRs that replace the corresponding amino acids in the acceptor immunoglobulin light chain framework, and each of these said donor amino acids is capable of interacting with the CDRs.

97. (New) A humanized immunoglobulin according to any one of claims 93 through 96, wherein said humanized immunoglobulin is an antibody tetramer, Fab, or $(Fab')_2$.

98. (New) A humanized immunoglobulin according to any one of claims 93 through 96, which is substantially pure.

99. (New) A pharmaceutical composition comprising a humanized immunoglobulin according to claim 98 and a pharmaceutically acceptable carrier.

100. (New) A humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from human acceptor immunoglobulin heavy and light chain frameworks, which humanized immunoglobulin specifically binds to an antigen with an affinity constant of at least about 10^8 M^{-1} and no greater than about four-fold that of the donor immunoglobulin, wherein the sequence of the acceptor immunoglobulin heavy chain variable region framework is at least 65% identical to the sequence of the donor immunoglobulin heavy chain variable region framework and the humanized immunoglobulin heavy chain variable region framework comprises at least 70 amino acids identical to those in a human immunoglobulin heavy chain variable region framework, wherein the percentage of sequence identity is determined by aligning amino acids in said frameworks by Kabat numbering.

101. (New) A humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from human acceptor immunoglobulin heavy and light chain frameworks, which humanized immunoglobulin specifically binds to an antigen with an affinity constant of at least about 10^8 M^{-1} and no greater than about four-fold that of the donor immunoglobulin, wherein the sequence of the acceptor immunoglobulin heavy chain variable region framework is at least 70% identical to the sequence of the donor immunoglobulin heavy chain variable region framework and the humanized immunoglobulin heavy chain variable region framework comprises at least 70 amino acids identical to those in a human immunoglobulin heavy chain variable region framework, wherein the percentage of sequence identity is determined by aligning amino acids in said frameworks by Kabat numbering.

102. (New) A humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from human acceptor immunoglobulin heavy and light chain frameworks, which humanized immunoglobulin specifically binds to an antigen, wherein the sequence of the acceptor immunoglobulin heavy chain variable region framework is at least 65% identical

to the sequence of the donor immunoglobulin heavy chain variable region framework, and the humanized immunoglobulin heavy chain variable region framework comprises at least 70 amino acids identical to those in a human immunoglobulin heavy chain variable region framework, wherein the percentage of sequence identity is determined by aligning amino acids in said frameworks by Kabat numbering.

103. (New) A humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from human acceptor immunoglobulin heavy and light chain frameworks, which humanized immunoglobulin specifically binds to an antigen, wherein the sequences of the acceptor immunoglobulin heavy and light chain variable region frameworks are respectively at least 65% identical to the sequences of the donor immunoglobulin heavy and light chain variable region frameworks, and the humanized immunoglobulin heavy and light chain variable region frameworks respectively comprise at least 70 amino acids identical to those in human immunoglobulin heavy and light chain variable region frameworks, wherein the percentage of sequence identity is determined by aligning amino acids in said frameworks by Kabat numbering.

104. (New) A humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from human acceptor immunoglobulin heavy and light chain frameworks, which humanized immunoglobulin specifically binds to an antigen, wherein the sequences of the acceptor immunoglobulin heavy and light chain variable region frameworks are respectively at least 70% identical to the sequences of the donor immunoglobulin heavy and light chain variable region frameworks, and the humanized immunoglobulin heavy and light chain variable region frameworks respectively comprise at least 70 amino acids identical to those in human immunoglobulin heavy and light chain variable region frameworks, wherein percentage sequence identity is determined by aligning amino acids in said frameworks by Kabat numbering.